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Percutaneous access to the uterus for fetal surgery.

VanderWall KJ, Meuli M, Szabo Z, Bruch SW, Kohl T, Hoffman WY, Adzick NS, Harrison MR.

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In utero repair of selected life-threatening malformations in the human fetus is now a clinical reality, yet fetal surgery continues to pose significant risks to both the mother and the unborn child. Preterm labor is a major problem directly related to the large uterine incision required for fetal exposure. Using technology developed for laparoscopic surgery, we have devised instruments and techniques to perform fetal endoscopic surgery. We now report a percutaneous technique for direct endoscopic access to the uterus. Minimally invasive fetoscopic surgery may expand the indications for fetal surgery by decreasing fetal risks, facilitating intervention earlier in gestation, and reducing preterm labor. This technique was developed in 4 fetal lambs who underwent endoscopic intervention at 105-110 days gestation (term = 145 days). Under ultrasound guidance, a 20-gauge spinal needle was advanced through the maternal abdomen, uterus, and directly into the amniotic cavity. Warmed saline was infused through the needle to expand the amniotic cavity. Next, a 5-mm balloon-tipped trocar was placed percutaneously with ultrasound guidance into the amniotic cavity. A 5-mm laparoscope was introduced and under endoamniotic vision two more 5-mm trocars were percutaneously placed. In all four sheep a 5-mm trocar was placed percutaneously into the gravid uterus. The most difficult step was puncturing through the amniotic membranes, but the sharp tip of the trocar facilitated getting into the amniotic cavity. Excellent visualization of the fetus was obtained with minimal uterine trauma. We have developed a fetoscopic technique in sheep for percutaneous placement of trocars into the uterus using ultrasound guidance. This approach allowed excellent visualization of the fetus with significantly less uterine trauma than open fetal surgery and is an essential prerequisite for future fetal endoscopic interventions.

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Endoscopic intrauterine surgery in primates Overcoming technical obstacles

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Abstract:

Abstract. Current protocols for fetal surgery require cesarean section and partial fetal extraction, both of which impart significant risks to the mother and fetus. Endoscopic fetal surgery is less invasive and will likely reduce some of these risks, but the technical difficulties and feasibility in a primate model have yet to be explored fully. Four pregnant baboons (95 days gestation) were anesthetized, their uteruses exposed via an abdominal incision, and blunt-tipped flanged endoscopic ports inserted. Amniotic fluid was removed, and warmed saline was infused to dilate the uterus. To evaluate instrumentation and wound closure, the tip of the snout was externalized and bilateral cleft lip-like defects made. The lips were then endoscopically repaired by suture (Endostitch, U.S. Surgical) or unique nonpenetrating clips (VCS, U.S. Surgical). The saline was then removed, amniotic fluid returned, and the ports carefully removed. After 4 weeks, the fetuses were delivered and evaluated. Eight cleft lip-like defects were successfully repaired in all four cases. Operative time averaged 83 min. No infections, amniotic leaks, or adhesions developed. Survival was 50% with two fetuses delivering within 48 hours postoperatively: one from preterm labor, the other with fetal demise from retroperitoneal hemorrhage after operative blunt abdominal trauma. We demonstrate the feasibility of endoscopic fetal surgery in primates. The use of blunt-tipped flanged ports provides a fluid tight seal and allows appropriate closure of the fetal membranes, but requires laparotomy and uterine exposure. Distension of the uterus with warmed saline affords a larger operating field, enhancing visualization and instrumentation of the fetus. Grasping the fetus through the exposed uterus gives excellent control for repair. However, such control is also needed in a percutaneous approach. Further instrumentation development is needed to accomplish similar control for the percutaneous approach.

Keywords:

Key words: Fetal surgery — Endoscopy — Primate — Baboon — Cleft lip — Wound healing — Fetoscopy
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ANSWER 3 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2003012687 MEDLINE
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TITLE: Human fetal adrenal transplant: a possible role in relieving intractable pain in advanced rheumatoid arthritis.
AUTHOR: Bhattacharya N; Chhetri M K; Mukherjee K L; Das S Prasad; Mukherjee A; Bhattacharya M; Bhattacharya S
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AB BACKGROUND: The art of transplant surgery has gone a long way in establishing itself as an important discipline in medicine with the support of molecular biology, immunology, biochemistry, etc., as the ultimate treatment for the restoration of function of a failing organ. With the progressive increase in the life expectancy of human beings, there is an increasing discrepancy in the demand and supply of organ grafts. A less efficient alternative could be synthetic or mechanical grafts. Nucleated cell therapy, that is, cellular transplant, is a promising new area of study with its proven efficacy in neuro-degenerative disorders, hematopoietic disorders, diabetes and trauma-induced tissue loss, to name a few. Human fetal cell/tissue with its intrinsic hypo-antigenic advantage (up to 20 weeks of study), could be an interesting area of cellular/tissue transplant. Our research group has earlier reported on the safe use of umbilical cord whole blood and the **successful** transplant of a human fetal lung, heart, pancreas, liver, thymus, in an artificially prepared vascular **subcutaneous** axillary fold in which there was no feature of hyper-acute, acute or chronic rejection of the graft in HLA- and sex-randomized adult recipients, without concomitant immunosuppressives or radiation of the host to potentiate the survival of the fetal graft (within 20 weeks of gestation) within the lowest observation period of one month. The present study was aimed at examining the role of developing fetal adrenal transplants for patients with rheumatoid arthritis and severe pain due to involvement of inflammatory and neuropathic components. MATERIALS AND METHOD: Ten cases were enrolled in the present study after thorough informed consent and approval by the ethical committee of the institute. The age of the patients varied from 50 to 76 years and the group was comprised of three males and seven females. The age of the adrenal grafts varied from 16 to 20 weeks and these were collected from mothers admitted for hysterotomy and ligation. These long-standing rheumatoid patients (suffering for five to 15 years), presented with at least four of the seven 1987 revised criteria of the American College of Rheumatology for diagnosis of rheumatoid arthritis. A 2.5 cm long and 2 cm deep tissue space was dissected and prepared in each transplant recipient at the axilla using diathermy and knife after infiltrating the site with one percent lignocaine solution. The tissue collected from the consenting mother undergoing hysterotomy and ligation was inserted into this site, and the site was closed with 00 atraumatic vicryl. All necessary pre- and postoperative surgical precautions were taken to prevent infections. Sequential total count and differential count of leucocytes were undertaken to analyze the impact of the transplant on the host. After one month, a part of the transplanted **fetal tissue** was recovered for histological staining to examine whether there was any graft versus host reaction. RESULTS AND ANALYSIS: All ten patients tolerated the transplant procedure well. There was no fever, intractable pain or any other specific serious side-effect which could justify the **removal** of the transplant before one month. There was no discharge from the incision site and the healing of the scar was by and large normal. There was no unusual leucocytosis, lymphocytosis and the retrieved graft tissue did not suggest transplant rejection. However,

there was definite pain relief, reduction in swelling and improvement of mobility of varying degree in a majority of the patients which was perceivable from the 15th day onwards. There was also a sense of well being (in 80%) and a gain in weight of three pounds or more (in 70%) among the fetal transplant recipients. DISCUSSION AND CONCLUSION: To understand the underlying mechanism, in case of pregnancy immunotolerance, we are of the opinion that emphasis should be placed on the role of non-specific and non-cytopathic blocking antibodies produced during pregnancy. The hypo-antigenicity of the developing human fetal system may possibly contribute to the production of this blocking antibody during pregnancy, and thus may play a role in the lack of recognition by the host's HLA system. This behaviour of the developing human **fetal tissue** provides some advantages over adult tissue for fetal cell/tissue transplantation purposes. The relief of pain, inflammation and restoration of mobility may be due to the effect of the transplanted adrenal graft, with the medullary component contributing to endorphin-like substance liberation and the cortical component contributing to glucocorticoid synthesis.

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on STN DUPLICATE 1

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AUTHOR: Rosser A.E.; Barker R.A.; Armstrong R.J.E.; Elneil S.; Jain M.; Hurelbrink C.B.; Prentice A.; Carne C.; Thornton S.; Hutchinson H.; Dunnett S.B.
CORPORATE SOURCE: A.E. Rosser, School of Biosciences, Cardiff University, Museum Avenue, Cardiff CF10 3US, United Kingdom. RosserAE@cf.ac.uk
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AB **Transplantation** of human fetal central nervous system tissue has been shown to be of benefit in Parkinson's disease, and is currently being explored as a therapeutic option in Huntington's disease. The **success** of a neural **transplant** is dependent on a number of factors, including the requirement that **donor** cells are harvested within a given developmental window and that the cell preparation protocols take account of the biological parameters identified in animal models. Although many of the criteria necessary for a **successful** neural **transplant** have been defined in animal models, ultimately they must be validated in human studies, and some issues can only ever be addressed in human studies. Furthermore, because neural **transplantation** of human **fetal tissue** is limited to small numbers of patients in any one surgical center, largely due to practical constraints, it is crucial that tissue preparation protocols are clearly defined and reproducible, so that (i) multicenter trials are possible and are based on consistent tissue preparation parameters, and (ii) results between centers can be meaningfully analyzed. Here we describe the preparation of human fetal striatum for neural **transplantation** in Huntington's disease, and report on the validation of a method for estimating the developmental stage of the fetus based on direct morphometric measurements of the embryonic tissue.